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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/565,736

04/19/2006

Sunil Govindrao Uttarwar

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04/04/2008

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EXAMINER

CHANDRAKUMAR, NIZAL S

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

04/04/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/565,736	Applicant(s) UTTARWAR ET AL.	
	Examiner NIZAL S. CHANDRAKUMAR	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02/26/2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 26-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>07/11/2006; 04/19/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application filed 04/19/2006 is a 371 of PCT/GB04/03209 07/23/2004.

Claims 1-31 are pending; claims 32-38 cancelled.

Election/Restrictions

Applicant's election with traverse of Group I, drawn to process of purifying citalopram in the reply filed on 02/19/2008 is acknowledged. Applicant's argument with respect to claims 24 and 25 is persuasive and as such the restriction requirement with respect to these claims is withdrawn. Applicant does not traverse the restriction with respect to other claims.

Claims 26-31 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 02/19/2008.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites polybasic acid without defining what polybasic acids protection is sought for. The nature of the polybasic acid is of relevance because the impurities being removed have similar basicity as that of citalopram. The pH of the extracting solutions is an essential element in the process of

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purification because the impurities and the product being purified citalopram is also basic. Further confusing is the recitation of 'strength' of the polybasic acid, in a manner unusual in the art. Acid strength is generally defined in terms of normality or molarity or concentration. The absence of disclosure with respect to the polybasic acid makes the assessment of the strength of the acid needed vague further in view of the recitation of a wide range.

The definition of the term 'strength' is also vague in the specification wherein the term appears in paragraph [0035] and [0036]. A close examination of the concentration of the polybasic used in the working examples 1-3 further raises additional questions discussed in rejection under 35 U.S.C. 112.

Recitation of specific polybasic acid(s) and the concentration(s)s commensurate with enabled disclosure would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim1 and dependent claims rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the purification of citalopram under well defined conditions using one polylbasic acid or salt at one specific concentration, does not reasonably provide enablement for obtaining pure citalopram from 'crude mixture' of citalopram prepared by any method using any polybasic acid. The specification is enabling for purifying Citalopram, for example prepared by the method of cyclization of dihydroxy compound using polybasic acid disodium edetate. The same method would not be available with the use citric acid or it salt as polybasic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention as claimed commensurate in scope with these claims. The vague definitions of the concentration of the polybasic acid, in the context the working examples present in the specification render the claims unpredictable. For example, in the working Example-1, a crude solution containing citalopram is washed

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with 5% disodium edetate twice. This step allegedly removes the carboxamide impurity (resulting from hydrolysis of the cyano group of the starting material) and cyano diol impurity (i.e., starting material). The organic phase now contains citalopram, which is ultimately isolated in purity of greater than 99.85%. Thus in this example, the wash with 5% disodium edetate does not remove citalopram from the organic phase. The process of Example-2 on the other hand, uses the same strength of 5% disodium edetate to wash an organic solution containing citalopram, but this time, the citalopram gets into the aqueous phase from which it is recovered in purity of greater than 99.85%. Thus at one time, the polybasic acid at the given concentration is able to selectively remove 'impurity' and at another time the same polybasic acid at the same concentration dissolves citalopram. Given that yield information is absent in the disclosed Examples, it is unpredictable what impurity can be removed with this process. The specification contains a list of potential contaminants, in 'crude mixtures' of citalopram preparations, in the descending order of basicity, wherein citalopram is placed somewhere in the middle (see page 2). Thus, presumably, the most basic of the impurity, 5-carboxamide citalopram would be the first one to be removed with the first acid wash. However, this wash does not limit the loss of citalopram. Absent information relating to the yield of the process, the efficiency is highly unpredictable. Further, it is unpredictable whether 5-formyl citalopram and descyano citalopram placed just above and below citalopram in the basicity scale, could be removed by this process. Likewise, the direction provided in the working Example-3 is confusing because the role of ethylene diamine washes are unclear and as in the Example-2, washing with 5% disodium edetate dissolves citalopram into the aqueous phase as opposed to the guidance provided in the Example-1 wherein 5% disodium edetate does not dissolve citalopram.

Thus the direction, guidance and working example disclosed in the specification is unpredictable as to the applicability of the claimed process commensurate with the scope of the claim. The enablement is limited to the purification of citalopram under narrowly disclosed conditions specific to 1) method of preparation of the citalopram 2) specific polybasic acid 3) specific concentration 4) specific washing procedure with regards to amount of extracting phases etc.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent

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protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Limiting the particulars of the process as indicated above as per the Examples 1-3, would overcome the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 and dependent claims rejected under 35 U.S.C. 103(a) as being unpatentable over Coppi et al (US 6635773) and Satyanarayana et al (GB 2375 763 A).

Coppi et al teach a process for preparing purified citalopram or one of its salts that comprises the purification of citalopram by selective extractions of citalopram or of its impurities with organic solvents and water under specific conditions of pH (5.8 to 6.3) and temperature. The crude citalopram can be prepared by a process that comprises reacting 1-[3-(dimethylamine)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-bromoisobenzofuran with copper cyanide.

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Satyanarayana et al. teach process for preparing purified citalopram by formation of citalopram salts, such as the oxalate, and repeated basification and salt formation and manipulation of pH for removing selected impurities.

Coppi et al. and Satyanarayana et al. do not teach the limitations of the instant claim such as the use of polybasic acid and or the range of the 'strength' of the acid (see rejection under 35 U.S.C. 112 second and first paragraph) for washing organic solutions as instantly claimed.

However one skilled in the art, attempting to arrive at alternate forms of purification of commercially important citalopram would be motivated to modify the extraction procedures with alternate acids to adjust the pH and temperature for extractions with reasonable expectation of success because Coppi et al teach that at specific conditions of pH and temperature, citalopram could be purified free of impurities.

Likewise, the teachings of Satyanarayana et al. for the purification by washing the organic phase with polybasic acid (oxalic acid) to selectively remove impurities from crude mixtures containing citalopram were clearly in front of the applicant at the time of the application. Optimizing process by using alternate acid washes to remove basic impurities and optimizing pH within ranges taught in the prior art, are within the routine nature in the practice of chemical process development. Thus, "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nizal S. Chandrakumar

/D. Margaret Seaman/

Primary Examiner, Art Unit 1625